A novel dual-color reporter for identifying insulin-producing beta-cells and classifying heterogeneity of insulinoma cell lines.

Journal: PLoS One

Publication Year: 2012

Authors: Nan Sook Lee, Joyce G Rohan, Madison Zitting, Sonia Kamath, Andrew Weitz, Arnold Sipos, Paul M Salvaterra, Kouichi Hasegawa, Martin Pera, Robert H Chow

PubMed link: 22530041

Funding Grants: CIRM Stem Cell Biology Training Grant

Public Summary:
We expect that our reporter will facilitate easy and quick evaluation of new differentiation protocols designed to produce clinically useful beta-cells—it could be stably introduced into human pluripotent stem cells or transduced into different stage cells using an adenoviral vector. In addition, the reporter system may be used as a high-throughput screening for reprogramming non-insulin-producing cells to insulin-producing cells.

Scientific Abstract:
Many research studies use immortalized cell lines as surrogates for primary beta- cells. We describe the production and use of a novel "indirect" dual-fluorescent reporter system that leads to mutually exclusive expression of EGFP in insulin-producing (INS(+)) beta-cells or mCherry in non-beta-cells. Our system uses the human insulin promoter to initiate a Cre-mediated shift in reporter color within a single transgene construct and is useful for FACS selection of cells from single cultures for further analysis. Application of our reporter to presumably clonal HIT-T15 insulinoma cells, as well as other presumably clonal lines, indicates that these cultures are in fact heterogeneous with respect to INS(+) phenotype. Our strategy could be easily applied to other cell- or tissue-specific promoters. We anticipate its utility for FACS purification of INS(+) and glucose-responsive beta-like-cells from primary human islet cell isolates or in vitro differentiated pluripotent stem cells.